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TITLE: Processing of bacterial antigens for peptide presentation on MHC class I molecules.

AUTHORS: Wick MJ; Ljunggren HG

AUTHOR AFFILIATION: Department of Cell and Molecular Biology, Lund University, Sweden. mary_jo.wick@immuno.lu.se

SOURCE: Immunol Rev 1999 Dec;172:153-62

CITATION IDS: PMID: 10631944 UI: 20097562

ABSTRACT: Professional antigen-presenting cells (pAPC) can process and present exogenous antigens on major histocompatibility complex class I (MHC-I) molecules. This unusual pathway for antigen presentation may represent a physiologically important step in the course of priming and tolerance induction of CD8+ T cells. In addition, it may play an important role in immunological surveillance for pathogens that survive in vacuolar compartments in APC. The goal of the present review is to discuss recent studies on the processing of bacterial-derived antigens for presentation on MHC-I molecules. The antigen presentation emphasized will include bacteria that remain confined in vacuolar compartments. This is in contrast to antigens derived from bacteria that have intrinsic properties allowing translocation across membranes and access into the classical MHC-I presentation pathway. In particular, presentation of bacterial antigens by dendritic cells (DC) will be emphasized, and MHC-I presentation of antigens derived from apoptotic cells, particularly cells induced to undergo apoptosis by microbial infection, will be presented. Finally, some special aspects of the interaction between bacteria and DC will be discussed as it relates to DC maturation, antigen presentation and T-cell stimulation.

MAIN MESH HEADINGS: *Antigen Presentation
Antigens, Bacterial/*metabolism
Histocompatibility Antigens Class I/*metabolism

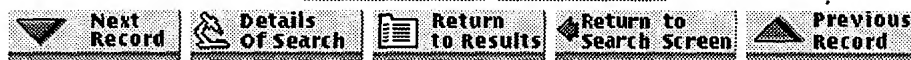
ADDITIONAL MESH HEADINGS: Animal
Antigen-Presenting Cells/immunology

Apoptosis/immunology
Dendritic Cells/immunology
Human
Macrophages/immunology
Models, Biological
Peptides/immunology
Peptides/metabolism
Salmonella typhimurium/immunology
Signal Transduction
Support, Non-U.S. Gov't
2000/02
2000/19 09:00

PUBLICATION TYPES: JOURNAL ARTICLE
REVIEW
REVIEW, TUTORIAL

CAS REGISTRY 0 (Antigens, Bacterial)
NUMBERS: 0 (Histocompatibility Antigens Class I)
0 (Peptides)

LANGUAGES: Eng



REVIEW
REVIEW, TUTORIAL

CAS REGISTRY NUMBERS: 0 (beta 2-Microglobulin)
0 (calreticulin)
0 (tapasin)
0 (Antiporters)
0 (Calcium-Binding Proteins)
0 (Histocompatibility Antigens Class I)
0 (Immunoglobulins)
0 (Peptides)
0 (Ribonucleoproteins)

LANGUAGES: Eng

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AI42793/AI/NIAID
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National Library of Medicine: IGM Full Record Screen

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to ResultsReturn to
Search ScreenPrevious
Record[Related Articles](#)[External Links](#)**TITLE:**

Structural features of MHC class I molecules that might facilitate alternative pathways of presentation.

AUTHORS:

Hansen T; Balendiran G; Solheim J; Ostrov D; Nathenson S

AUTHOR AFFILIATION:

Washington University School of Medicine, St Louis, MO 63110, USA. hansen@genetics.wustl.edu

SOURCE:

Immunol Today 2000 Feb;21(2):83-8

CITATION IDS:

PMID: 10652466 UI: 20119147

ABSTRACT:

Comparisons of the structures of different mouse MHC class I molecules define how polymorphic residues determine the unique structural motif and atomic anchoring of their bound peptides. Here, Ted Hansen and colleagues speculate that quantitative differences in how class I molecules interact with peptide, beta2-microglobulin and molecular chaperones that facilitate peptide loading might determine their relative participation in different pathways of antigen presentation.

MAIN MESH HEADINGS:

*Antigen Presentation
Histocompatibility Antigens Class I/*chemistry
Histocompatibility Antigens Class I/*physiology

ADDITIONAL MESH HEADINGS:

beta 2-Microglobulin/metabolism
Animal
Antigen Presentation/immunology
Antiporters/metabolism
Calcium-Binding Proteins/metabolism
Histocompatibility Antigens Class I/metabolism
Immunoglobulins/metabolism
Mice
Molecular Conformation
Peptides/metabolism
Ribonucleoproteins/metabolism
Support, U.S. Gov't, P.H.S.
2000/03
2000/11 09:00

PUBLICATION TYPES:

JOURNAL ARTICLE

PROCESSING COMPLETED FOR L5
L6 3 DUP REM L5 (3 DUPLICATES REMOVED)

=> dis 16 1-3 kwic

- L6 ANSWER 1 OF 3 MEDLINE DUPLICATE 1
AB . . . thymocytes differentiate into T lymphocytes when co-cultured with mouse fetal thymic organs. Hematopoietic stem cells for myeloid and thymic stromal **dendritic** cells (DCs) are present within the minute population of CD34+ progenitors within the mammalian thymus. The common myeloid, DC, natural. . . reticuloendothelial system (RES) and DCs represent the cellular mediators of these regulatory endocrine-immune interactions. Folliculo-stellate cells (FSC) in the AP, **Langerhans** cells (LCs) in the skin and lymphatic system, "veiled" cells, lympho-**dendritic** and interdigitating cells (IDCs) in a number of tissues comprising the lymphatic system are the cell types of the DC meshwork of "professional" **antigen presenting cells** (APCs). Most of these cells express the immunocytochemical markers S-100, CD1. CD45, CD54, F418, **MHC class I** and II antigens, Fc and complement receptors. FSCs are non-hormone secreting cells which communicate directly with hormone producing cells, a. . . identified as the interferon-gamma responsive elements. FSCs also express lymphatic DC markers, such as DC specific aminopeptidase, leucyl-beta-naphthylaminidase, non-specific esterase, **MHC class I** and II molecules and various other lymphatic immunological determinants [platelet derived growth factor-alpha chain (PDGF-alpha chain), CD13, CD14 and L25. . . endocytic compartment, MIIC (MHC class II-enriched compartment), that harbors newly synthesized MHC class II antigens en route to the cell **membrane**. The limiting **membrane** of MIIC can fuse directly with the cell **membrane**, resulting in release of newly secreted intracellular MHC class II antigen containing vesicles (**exosomes**). DCs possess the ability to present foreign peptides complexed with the MHC molecules expressed on their surfaces to naive and. . .
- L6 ANSWER 2 OF 3 CAPLUS COPYRIGHT 2000 ACS
AB The authors have previously shown that Bordetella pertussis CyaA adenylate cyclase toxin can be used as a **vehicle** to deliver T-cell epitopes (inserted within the catalytic domain) into **antigen-presenting cells** and can trigger specific **MHC class I**-restricted CD8+ T-cell responses in vivo. To examine the role of charges in CyaA translocation, the authors constructed a set of. . . was crit. for its translocation within eukaryotic cells. These results suggest that CyaA uses the elec. field across the plasma **membrane** as a driving force to enter into target cells.
- L6 ANSWER 3 OF 3 EMBASE COPYRIGHT 2000 ELSEVIER SCI. B.V.
AB We have shown that growth factor-dependent, **MHC class I+/II- dendritic** cell lines established from mouse fetal skin, can stimulate naive, allogeneic but not syngeneic CD8+ T cells in the absence of CD4+ T cells and that this T cell response is restricted by **MHC class I** molecules. We further showed that the FSCKL-induced activation of naive CD8+ T cells is critically dependent on the physical contact. . . are members of the LC/DC family because they (i) exhibit certain features of fetal murine LC (i.e., CD45+, CD44+, CD32+, **MHC class I+**, **MHC class II-**, asialo GM1+, TCR-) including **membrane-bound** ADPase activity (A. Elbe, unpublished observation) and (ii) exhibit a pronounced **dendritic** configuration when cultured. If these cells are indeed derived from fetal LC, they should undergo the same phenotypic changes (MHC. . . maturation process would not have been completed. Alternatively, the attractive possibility exists that we have generated a population of 'mature' **MHC class I+/II-** cells, which, perhaps because of their paucity, have so far escaped in vivo detection by conventional immunolabeling procedures. Evidence for the latter hypothesis comes from studies by Sprent et al. and Holt et al. (3rd) International Symposium on **Dendritic** Cells in Fundamental and Clinical Immunology), who described the existence of MHC class II-**antigen presenting cells** in the spleen, bone marrow, and fetal liver by functional criteria, and of **MHC class I+/II-** DC in situ in the conducting airways,

respectively. While in this study FSCL were used for all-sensitizing purposes, it is not unreasonable to assume that they can also function as potent **vehicles** for the induction of primary responses against nominal antigens. As such, they may be ideally suited to study (i) the **MHC class I**-associated immunogenicity of selected (tumor, viral) peptide antigens and (ii) to generate CD8+ immune responses, in vitro and in vivo, against. . .

=> dis 16 1-3

L6 ANSWER 1 OF 3 MEDLINE DUPLICATE 1
 AN 97437770 MEDLINE
 DN 97437770
 TI Dendritic type, accessory cells within the mammalian thymic microenvironment. Antigen presentation in the dendritic neuro-endocrine-immune cellular network.
 AU Bodey B; Bodey B Jr; Kaiser H E
 CS Department of Pathology, School of Medicine, University of Southern California, Los Angeles, USA.
 SO IN VIVO, (1997 Jul-Aug) 11 (4) 351-70.
 Journal code: A6F. ISSN: 0258-851X.
 CY Greece
 DT Journal; Article; (JOURNAL ARTICLE)
 LA English
 FS Priority Journals
 EM 199712
 EW 19971204

L6 ANSWER 2 OF 3 CAPLUS COPYRIGHT 2000 ACS
 AN 1998:419480 CAPLUS
 DN 129:188079
 TI Translocation of Bordetella pertussis adenylate cyclase toxin into eukaryotic cells: role of charges
 AU Ladant, D.; Karimova, G.; Fayolle, C.; Leclerc, C.; Ullmann, A.
 CS Unite de Biochimie Cellulaire, Institut Pasteur, Paris, 75724, Fr.
 SO Zentralbl. Bakteriол., Suppl. (1997), 29(Bacterial Protein Toxins), 146-147
 CODEN: ZBASE2; ISSN: 0941-018X
 PB Gustav Fischer Verlag
 DT Journal
 LA English

L6 ANSWER 3 OF 3 EMBASE COPYRIGHT 2000 ELSEVIER SCI. B.V.
 AN 95276215 EMBASE
 DN 1995276215
 TI Dendritic cells as stimulator cells of MHC class I-restricted immune responses.
 AU Elbe A.; Stingl G.
 CS Div. of Immunology, Department of Dermatology, Univ. of Vienna Medical School, Vienna, Austria
 SO Advances in Experimental Medicine and Biology, (1995) 378/- (341-345).
 ISSN: 0065-2598 CODEN: AEMBAP
 CY United States
 DT Journal; Conference Article
 FS 025 Hematology
 026 Immunology, Serology and Transplantation
 LA English
 SL English

=> dis 16 1-3 abs

L6 ANSWER 1 OF 3 MEDLINE DUPLICATE 1
 AB During mammalian ontogenesis, the thymic "pure" endodermal epithelial anlage develops and differentiates into a complex cellular microenvironment. Beginning the 7-8th week of intrauterine development, thymic epithelial cells chemotactically regulate (induce) numerous waves of migration of stem cells into the thymus, including the CD34+, yolk sac-derived, committed hematopoietic stem cells. In vitro experiments have established that CD34+ CD38dim human thymocytes differentiate into T lymphocytes when co-cultured with mouse fetal thymic organs. Hematopoietic stem cells for myeloid and thymic stromal **dendritic** cells (DCs) are present within the minute population of CD34+ progenitors within the mammalian thymus. The common myeloid, DC, natural killer (NK) and T lymphocyte progenitors have also been identified within the CD34+ stem cell population in the human thymus. Interactions between the endocrine and immune systems have been reported in various regions of the mammalian

body including the anterior pituitary (AP), the skin, and the central (thymus) and peripheral lymphatic system. The network of bone marrow derived DCs is a part of the reticuloendothelial system (RES) and DCs represent the cellular mediators of these regulatory endocrine-immune interactions. Folliculo-stellate cells (FSC) in the AP, **Langerhans cells (LCs)** in the skin and lymphatic system, "veiled" cells, lympho-**dendritic** and interdigitating cells (IDCs) in a number of tissues comprising the lymphatic system are the cell types of the DC meshwork of "professional" **antigen presenting cells** (APCs). Most of these cells express the immunocytochemical markers S-100, CD1, CD45, CD54, F418, **MHC class I** and II antigens, Fc and complement receptors. FSCs are non-hormone secreting cells which communicate directly with hormone producing cells, a form of neuro-endocrine-immune regulation. As a result, an attenuation of secretory responses follows stimulation of these cells. FSCs are also the cells in the AP producing interleukin-6 (IL-6), and they have also been identified as the interferon-gamma responsive elements. FSCs also express lymphatic DC markers, such as DC specific aminopeptidase, leucyl-beta-naphthylaminidase, non-specific esterase, **MHC class I** and II molecules and various other lymphatic immunological determinants [platelet derived growth factor-alpha chain (PDGF-alpha chain), CD13, CD14 and L25 antigen]. There is strong evidence that such DCs in the AP, and similar ones in the developing thymus and peripheral lymphatic tissue are the components of a powerful "professional" antigen presenting DC network. These APCs contain a specialized late endocytic compartment, MIIC (MHC class II-enriched compartment), that harbors newly synthesized MHC class II antigens en route to the cell **membrane**. The limiting **membrane** of MIIC can fuse directly with the cell **membrane**, resulting in release of newly secreted intracellular MHC class II antigen containing vesicles (**exosomes**). DCs possess the ability to present foreign peptides complexed with the MHC molecules expressed on their surfaces to naive and resting T cells. There are a number of "molecular couples" that influence DC and T lymphocyte interaction during antigen presentation: CD1/CD18 integrins, intercellular adhesion molecules (ICAMs), lymphocyte function associated antigen 3 (LFA-3). CD40, CD80/B7-1, CD86/B7-2, and heat-stable antigen. The "molecular couples" are involved in adhesive or co-stimulatory regulations, mediating an effective binding of DCs to T lymphocytes and the stimulation of specific intercellular communications. DCs also provide all of the known co-stimulatory signals required for activation of unprimed T lymphocytes. It has been shown that DCs initiate several immune responses, such as the sensitization of MHC-restricted T lymphocytes, resistance to infections and neoplasms, rejection of organ transplants, and the formation of T-dependent antibodies. (ABSTRACT TRUNCATED)

L6 ANSWER 2 OF 3 CAPLUS COPYRIGHT 2000 ACS

AB The authors have previously shown that Bordetella pertussis CyaA adenylate cyclase toxin can be used as a **vehicle** to deliver T-cell epitopes (inserted within the catalytic domain) into **antigen-presenting cells** and can trigger specific **MHC class I**-restricted CD8+ T-cell responses in vivo. To examine the role of charges in CyaA translocation, the authors constructed a set of recombinant toxins that harbor short peptide inserts with different charges. The results show that the electrostatic charge of the inserted peptides within the catalytic domain of CyaA was crit. for its translocation within eukaryotic cells. These results suggest that CyaA uses the elec. field across the plasma **membrane** as a driving force to enter into target cells.

L6 ANSWER 3 OF 3 EMBASE COPYRIGHT 2000 ELSEVIER SCI. B.V.

AB We have shown that growth factor-dependent, **MHC class I+II- dendritic** cell lines established from mouse fetal skin, can stimulate naive, allogeneic but not syngeneic CD8+ T cells in the absence of CD4+ T cells and that this T cell response is restricted by **MHC class I** molecules. We further showed that the FSCKL-induced activation of naive CD8+ T cells is critically dependent on the physical contact between stimulator and responder cells and the expression of the costimulatory molecule B7 on FSCL. An important question that remains to be addressed concerns the derivation of FSCL. One could argue that they are members of the LC/DC family because they (i) exhibit certain features of fetal murine LC (i.e., CD45+, CD44+, CD32+, **MHC class I+**, **MHC class II-**, asialo GM1+, TCR-) including **membrane-bound** ADPase activity (A. Elbe, unpublished observation) and (ii) exhibit a pronounced **dendritic** configuration when cultured. If these cells are indeed derived from fetal LC, they should undergo the same phenotypic changes (MHC class II- .fwdarw. MHC class II+) under in vitro culture conditions as do fetal LC in situ. However, our FSCL are phenotypically stable, and attempts to induce MHC class II expression with cytokine cocktails were

unsuccessful. One explanation for this phenomenon could be that stimulatory signals provided by fetal keratinocytes or other skin cells are responsible for LC maturation in vivo and that, due to the early demise of these 'stromal' cells in fetal skin cell cultures, the maturation process would not have been completed. Alternatively, the attractive possibility exists that we have generated a population of 'mature' **MHC class I+/II-** cells, which, perhaps because of their paucity, have so far escaped in vivo detection by conventional immunolabeling procedures. Evidence for the latter hypothesis comes from studies by Sprent et al. and Holt et al. (3rd) International Symposium on **Dendritic Cells** in Fundamental and Clinical Immunology), who described the existence of **MHC class II- antigen presenting cells** in the spleen, bone marrow, and fetal liver by functional criteria, and of **MHC class I+/II-** DC in situ in the conducting airways, respectively. While in this study FSCL were used for all-sensitizing purposes, it is not unreasonable to assume that they can also function as potent **vehicles** for the induction of primary responses against nominal antigens. As such, they may be ideally suited to study (i) the **MHC class I-associated immunogenicity** of selected (tumor, viral) peptide antigens and (ii) to generate CD8+ immune responses, in vitro and in vivo, against such antigens.

=> dis his

(FILE 'HOME' ENTERED AT 11:47:09 ON 07 AUG 2000)

FILE 'MEDLINE, CAPLUS, EMBASE, BIOSIS' ENTERED AT 11:47:24 ON 07 AUG 2000

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L1      2 S (MHC (1N) CLASS (1N) I)
L2      29153 S (MHC (1N) CLASS (1N) I)
L3      5044 S L2 (P) ((B (1N) CELL) OR (ANTIGEN (1N) PRESENTING (1N) CELL)
L4      492 S L3 (P) MEMBRANE?
L5      6 S L4 (P) (VEHICLE? OR EXOSOME?)
L6      3 DUP REM L5 (3 DUPLICATES REMOVED)

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